2022

The advancement in 3D printing technology and its applications with bone grafting and dental implants

https://hdl.handle.net/2144/44002

BOSTON UNIVERSITY

SCHOOL OF MEDICINE

Thesis

THE ADVANCEMENT IN 3D PRINTING TECHNOLOGY AND ITS APPLICATIONS WITH BONE GRAFTING AND DENTAL IMPLANTS

by

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B.S., University of Massachusetts Lowell, 2019

Submitted in partial fulfillment of the
requirements for the degree of
Master of Science

2022

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DEDICATION

First and foremost, I dedicate this work to my patient and loving wife, Israh. I also dedicate this work to my family, advisors, mentors, and anyone who positively influenced my journey. Without their encouragement, kind words, support, and faith, I would not have progressed academically the way I have.

ACKNOWLEDGMENTS

I would like to thank Dr. Theresa A. Davies for being marvelous, altruistic, and compassionate. I cannot express my gratitude enough for all the support and help I received from her. I also would like to thank Dr. Maura Kelley for her exemplary contributions to my academic advancement. I am honored and privileged to be their student.

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AMR CHALABI

ABSTRACT

Since the late 20th century, breakthroughs in technology have been occurring expeditiously. Indeed, technological innovations have provided the betterment of many aspects of life and ensured humans' appropriate forms of evolution and civilization. It is safe to claim that medicine has advanced within the past few decades, especially with the upbringing of technological innovations. The world of medicine would not have experienced its recent breakthroughs and profound discoveries without utilizing the available technology.

The improvements observed in medicine and technology resulted in better providing of healthcare. Customizing treatments for each patient is now possible. One method of applying customization is through 3D printing of materials such as artificial prosthetics, tissues, and organs. This literature review analyzes 3D printing by stating definitions, assessing its history, discussing its different applications and closing with evaluating future directions.

3D printing first appeared in the late 20th century, and its primary purpose was to design and manufacture products efficiently and accurately. Traditional production of structures involves subtractive manufacturing (carving, cutting, and other methods of reshaping materials) to achieve desired products, whereas 3D

printers implement additive manufacturing (a layer-by-layer approach). This provides less time, greater accuracy, and labor-free fabrication of products. Computerized software is one of the essential parts of 3D printing, and functions include designing, scaling, visualizing, controlling production frequency, and many more. In medical applications, the software may require CT scans, cone beam computed tomography, and intraoral scanners (for dental applications).

The 3D printing techniques identified in this review are generally applied in oral and maxillofacial procedures—stereolithography, which constructs a product layer-by-layer through curing liquid resin using a UV laser. Digital light projection is a method similar to stereolithography, with a few differences, such as using a UV light instead of a laser and using a liquid crystal display panel. Fused deposition modeling is a technique that melts plastic filaments and extrudes them through a nozzle to form a structure in a layer-by-layer fashion. Selective laser sintering is also similar to stereolithography, where it uses a laser to form an object layer by layer, but the material is a thin layer of plastic powder instead of liquid resin. The power binder printing technique applies droplets onto powdered materials, adhering and forming layers as designed via computerized software. Lastly, computed axial lithography is similar to digital light projection, except the light is projected from many angles at once instead of one layer at a time.

The main objectives of this literature review are to investigate each technique, discuss the advantages and disadvantages, and list the commonly applied areas in medicine for each. Also, this review evaluates the current limitations experienced when using 3D printers and suggestions for overcoming them. Some limitations include, but are not limited to, excessive time allocated for producing specific structures, accurate capturing of surgical sites, use of appropriate materials that form printed structures, cost, and deficiencies of reported data.

Lastly, this literature review assesses the future projections. The future holds promising breakthroughs in 3D printing technology, including the fabrication of dental stem cells, operating artificial organs, complex vascular tissues, customized artificial alveolar structures for oral and intracranial procedures, and regeneration of periodontal tissues. These projections may occur by overcoming the most reported limitations.

Medicine is digitizing rapidly and will continue adapting to the latest technological inventions. The current efforts to advance 3D printing technology will likely positively impact the advancement of many fields, including healthcare, increase chances of positive postoperative outcomes, and potentially combat many health issues society faces today. Professionals across disciplines must come together to further research and educate curriculums to revolve around the innovative technologies to continuing education courses related to 3-D printing technologies.

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LIST OF ABBREVIATIONS

3D/4D	3-Dimensional/4-Dimensional
3DP	3-Dimensional Printing
ADA	American Dental Association
AM	Additive Manufacturing
CAD/CAM	Computer-Aided Design and Computer-Aided Manufacturing
CAL	Computed Axial Lithography
CBCT	Cone Beam Computed Tomography
DLP	Digital Light Projection
DMD	Digital Mirror Device
DTM	Desk Top Manufacturing
EBB	Electrospinning-Based Bioprinting
FDM	Fused Deposition Modeling
MFS	Maxillofacial Surgery
MJM	Multi-Jet Modeling
PBP	Power Binding Printer
PCL	Poly(ε-Caprolactone)
SM	Subtractive Manufacturing
SL	Stereolithography
SLA	Stereolithography Apparatus
SLS	Selective Laser Sintering
TiMe	Titanium Mesh

UV	Ultraviolet Light

INTRODUCTION

The rise of technological innovations in the sciences has been rapid. Almost all fields of knowledge and professions have advanced towards modern and trending technology with the intention of humanity's betterment, civilization, and preservation. Medicine has advanced significantly with the surpassing adaptation and utilization of the appropriate technological inventions. One factor that may have influenced the improvement of life expectancy within the past decades may be the furtherance of resources that lead to groundbreaking scientific and medical discoveries. Hence, healthcare providers and researchers have been able to examine, diagnose, treat, prevent, research, synthesize vaccines and medications, and perform many more actions to work towards improved health and healthy lifestyle among patients.

Most, if not all, professionals in medicine and natural sciences may agree on the existence of phenotypic and genotypic differences among all organisms due to genetic variations. Generalized protocols may be implemented when treating, for example, a particular disease or a case of trauma, but the uniqueness that each patient exhibits must not be ignored. Customizing treatments for each particular patient is essential for delivering the best healthcare, and said customization might occur through recent advances in medicine today, such as interprofessional collaboration, collaboration, cutting edge research in addition to technology. Thanks to technological advancement, 3D printing is one such method that has advanced the field of personalized or customized treatments. 3D printers are novel machinery, known as additive manufacturing. Its excitement has crossed to many fields beyond medicine but its initial usefulness in healthcare and continuing research and development will likely deliver stellar results in medicine moving forward.

BACKGROUND

Definitions:

3D printing is a technological innovation developed around the late 20th century to design and manufacture products in methods that ensure efficiency and practicality compared to typical production methods in many industries. The traditional production followed subtractive manufacturing (SM): carving solids of metals, plastic, or stones to produce a particular product (Min et al., 2018). 3D printing, however, adopts additive manufacturing (AM) that facilitates a layer-by-layer approach. Unlike subtractive manufacturing, 3D printing is rapid, accurate and enables creators to test a product's prototype before mass production. Using computerized software, a creator can design the desired product; then, printing machines fabricate the design (Min et al., 2018).

Recent research questions the contributions of 3D and 4D printing towards the improvement of oral procedures. It also questions its influence on maxillofacial surgery (MFS), which is the field in dental medicine that incorporates diagnosing and treating (via surgical and adjunctive treatments) impairments, deforms, illnesses, and other defects disrupting the functionality and the appearance of the oral and maxillofacial tissues (American Dental Association (ADA), 2018). In addition, the research on 3D/4D printing raised inquiries on the practicality of dental prosthetics produced via computer-aided design and computer-aided manufacturing (CAD/CAM). Groover and Zimmers (1983) define CAD as the utilization of computer software applications to design a product appropriately for the fabrication and production of a structure. CAM is the processing of inputs from computerized systems to execute plans made via CAD and administer the quality, quantity, frequency, and use of resources and materials available for manufacturing (Groover & Zimmers, 1983).

One article investigated the parties utilizing 3D and 4D printing, the products manufactured and their clinical manifestations in MFS, the source of production, and the effects of 3D/4D printing in dentistry (Louvrier et al., 2017). Their findings indicated that 3D printing was significantly beneficial since it improved oral and MFS precision and time spent performing procedures (Louvrier et al., 2017). Another study by Yen et al. (2018) suggests that further research projecting the effectiveness of 3D bioprinting products as time goes on is required. They claim they need additional research because the effectiveness results reported are limited. Also, the rapid advancement of 3D printing technology is ongoing. Lastly, the current data supporting the promising potential of CAD/CAM applications in fitted grafts for procedures involving alveolar ridge augmentation is insufficient (Yen et al., 2018).

As shown in Figure 1, various types of 3D/4D printing techniques are presently being exercised, according to Khorsandi et al. (2020). Stereolithography (SL), the initial form of 3D printing available commercially, adopts AM via "photoinduced polymerization," leading to the fabrication of resin products in a layer-by-layer fashion. Digital light projection (DLP) is similar to a stereolithography apparatus (SLA). The difference between DLP and SLA is that DLP uses liquid photosensitive materials that are photocured for solidification, using ultraviolet (UV) light from the apparatus's projector. SLA, however, contains a UV laser beam (Khorsandi et al., 2020). Fused deposition modeling (FDM) is the cheapest and second technique used after SLA, and it utilizes thermoplastic filaments by melting and applying layers of plastic one after the other. Selective laser sintering (SLS) uses a beam laser with great energy that induces the fusion of materials in a powdered form (Khorsandi et al., 2020).

The photopolymer jetting technology deploys a combination of photopolymerizable polymers and a dynamic inkjet-type printing head, leading to jetting the polymer onto a building platform in a descending fashion and using a supporting layer fabricated with fragile materials for removing printed products efficiently (Khorsandi et al., 2020). Power binder printer (PBP) applies adhesive droplets onto powdered materials to form the layers of the desired product. Lastly, computed axial lithography (CAL), a technique that is similar to DLP. The main difference is its polymerization method; the projected light is applied at different angles of the materials used for fabricating the product, whereas other AM techniques polymerize each layer individually (Khorsandi et al., 2020).

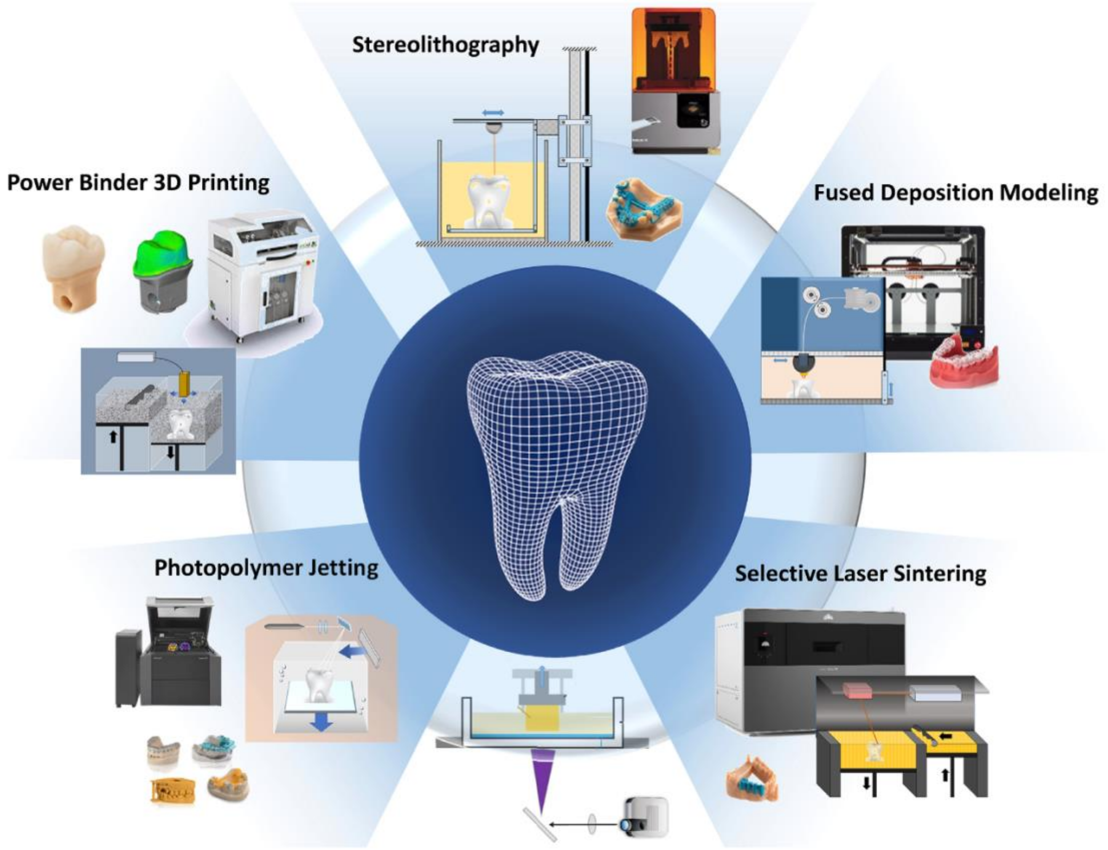


Figure 1: The Different 3D/4D Printing Techniques Used in Dental Applications. This figure projects various and current 3D printers; each adopts different methods for producing dental prosthetics, oral appliances, and artificial tooth-supporting tissues (crowns, bridges, implants, orthodontic appliances, and alveolar bone). (Figure taken from Khorsandi et al., 2020)

Other sources discuss the financial cost of manufacturing anatomic models using 3D printers. The reduction of operating room costs is successful with 3D printers' use by decreasing the amount of time spent performing surgical procedures, which is valuable to healthcare institutions in the long term (Ballard et al., 2019). Another article overviewed the multiple factors involved in calculating the mean cost of a 3D model used in orthognathic surgery; it costs $5.20 to fabricate a 3D model with a mean weight of 166.5g produced in about 12 hours (Narita et al., 2020).

3D-Printing History:

According to Ahn et al., a Japanese researcher named "Hideo Kodama" was an early innovator at the "Nagoya City Industrial Research Institute", where 3D printers were introduced in 1981. The revealed technology used photosensitive liquid resin that can be cured by UV light to create an object. With the utilization of a tank containing water, UV light, and a mask, the study was carried out on layering the photo-curable resin in the tank (Ahn et al., 2016). Ahn et al. stated that 3D systems by Hull created the first 3D printer in 1984, which conducted printing using the SLA technique. The Hull printer was similar to the technology used by Kodama, especially considering the exposure of materials to UV light. Hull's development of 3D Systems and printers was first introduced to the market in 1988. Following that, he coded software components essential to the printers, which consisted of a stereolithography file, and a CAD model file format; the format is currently being utilized in modern 3D printers (Ahn et al., 2016).

In 1986, Carl Deckard created an SLS 3D printer and was patented in 1989. Deckard then established a corporation called the "Desk Top Manufacturing" (DTM). In 2001, DTM merged with 3D Systems. In 1987, Larry Hornbeck, a physicist at Texas Instruments, developed a DLP printer that used a digital mirror device (DMD) to produce items via a curing method implementing repetition of exposure of liquid resin to UV light. In 1992, the inventor "Scott Crump" developed the FDM technique and filed its patent. Upon patenting, he established the Stratasys Company to launch FDM 3D printers to the market (Ahn et al., 2016).

In 1991, the patent for the photopolymer jetting technique was obtained by a Japanese party named "Brother Kogyo Kabushiki Kaisha". A year later, 3D Systems obtained a patent similar to the multi-beam modeling method. The Massachusetts Institute of Technology (MIT) was the first to develop and patent a PBP 3D printer in 1993. A corporation named "Z Corporation" was founded on the basis of the PBP's 3-dimensional printing (3DP) technology. In 1996, the Z Corporation filed for a patent on 3DP. Z Corporation became a part of 3D Systems in 2012 (Ahn et al., 2016).

Another article by Pravin and Sudhir (2018) confirms some of the facts that Ahn et al. (2016) stated in their article. Pravin and Sudhir added that in 1980, Dr. Hideo Kodama was the first to accomplish prototyping rapidly. Though he was considered a founding father for the AM technique, he failed in acquiring a patent for his work. Researchers accomplished the development of artificial organs in 1999, which provided new possibilities for the world of medical sciences. In 2000, scientists produced the first operational kidney through the breakthrough in 3D printers. However, attempts to transplant 3D-printed organs have not been reported due to the fact that research is still being conducted (Pravin and Sudhir, 2018).

3D Bioprinting History and Early Applications:

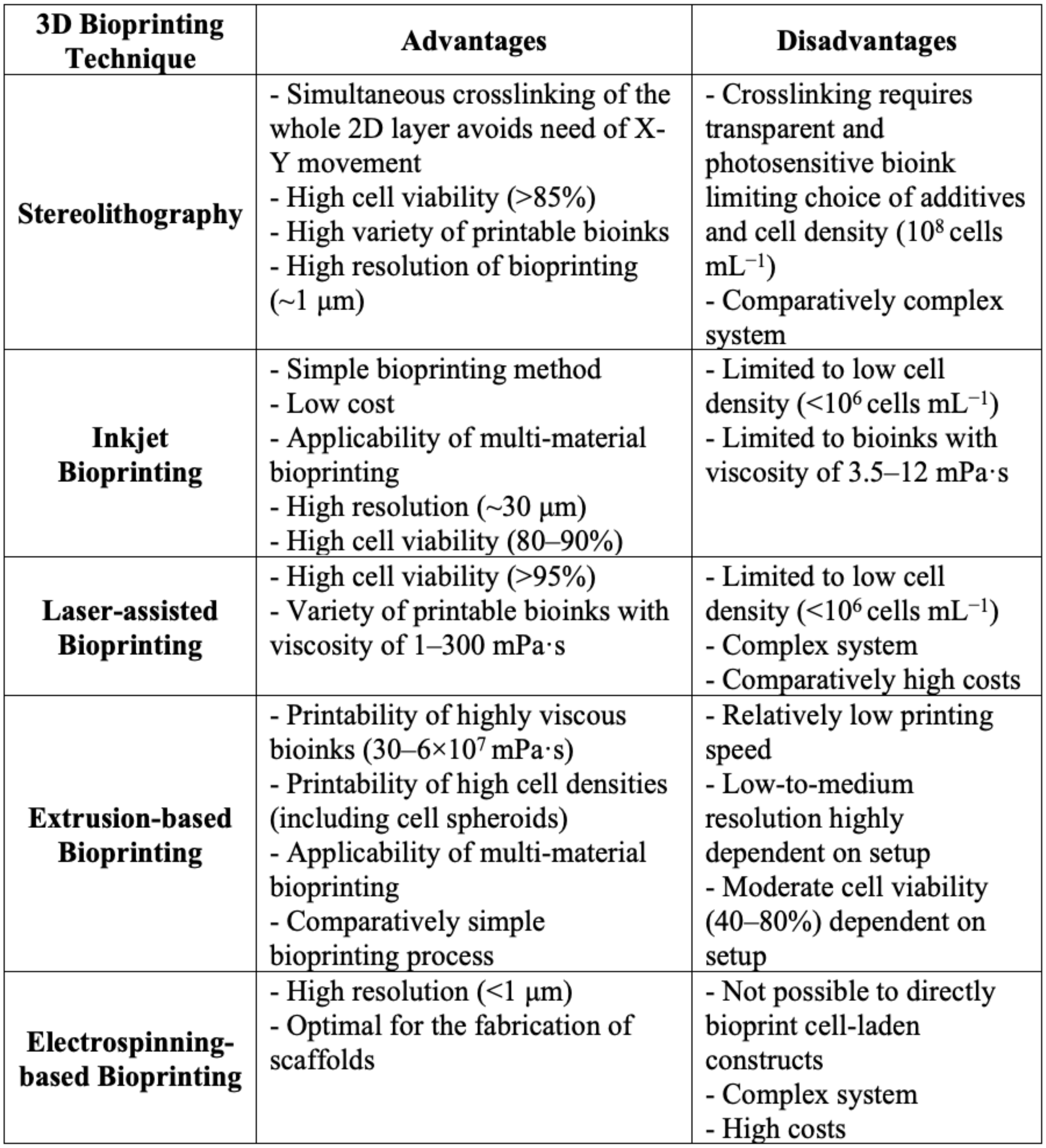
The advancement of 3D printing technology opened possibilities for achieving significant developments in medicine. It has been reported by Heinrich et al. (2019) that researchers have been utilizing the techniques available in the early 21st century for producing artificial tissues. Examples of those techniques include, but are not limited to, 3D scaffolding, microengineering (precisely the self-assembly-dependent form), fabrication of fiber, and cell sheet structuring via scaffold-free methods (Heinrich et al., 2019). Hydrogels and biodegradable polymers are the components that form scaffolds. The properties of the components enable scaffolds to be processed as appropriate foundations for engineered cells to perform their functions to achieve the desired goals of any artificial tissues (Heinrich et al., 2019). Also, microscale building units have the ability to construct masses similar in characteristics of the tissues in question. Building blocks such as cell-laden fibers may be utilized to form hierarchical structures through bonding strategies such as weaving or knitting. Furthermore, scaffold-free cell sheet structuring is conducted by piling up thin layers of cell sheets to mold appropriate tissues (Heinrich et al., 2019). It was concluded that the techniques mentioned earlier are deficient in great spatial precision and compliance, even though each technique has its advantages in specific applications (Heinrich et al., 2019).

Fortunately, the deficiencies were overcome upon the development of 3D bioprinting technology; software programs that generate production methods paved the way for researchers to implement accuracy and precision in producing, in significant amounts and an appropriate manner, cells and biomaterials in a volume observed in three dimensions (Heinrich et al., 2019). Figure 2 shows the different techniques applied in 3D bioprinting and images depicting the apparatuses of each kind of bioprinting method. Table 1 lists the differences in practicality between each 3D bioprinting method.

Stereolithography (SL) operates using an AM technique. In medicine, it was first dedicated to producing structures for reconstructive cranial surgeries with high accuracy and matching for detail. Heinrich et al. (2019) stated that SL might be at a disadvantage due to the need for the cell-laden bioink to be transparent with the least amount of dispersion, and failure in maintaining these conditions may cause the material to become less dense (Heinrich et al., 2019). The development and patenting of inkjet bioprinting occurred in 2003 and 2006, respectively. It operates by ejecting bioink on a 3-axis platform instead of a 2-axis paper and regular inkjet ink. The simplicity in the inkjet bioprinter’s operational system is an advantage that this technique has, not to mention the low cost. However, the density of cells produced is relatively low, in addition to its properties to print viscous products, according to Table 1. This kind of bioprinter produces artificial cartilage, vascular tissues, and certain bone types (Henrich et al., 2019).

In 2007, laser-assisted bioprinting made its first appearance. It is based on either laser direct-write or laser-induced forward transfer. Its apparatus is shown in Figure 2, and it has three layers: the top layer for absorbing energy (a precious metal, such as gold or titanium), the middle layer as a donor, and the thin bottom layer containing the bioink. The laser produces a beam at set locations, which gets absorbed by the top layer. The donor layer vaporizes, creating high-pressure bubbles that form bioink droplets to transfer onto a collection platter. An advantage of this method is that the bioink has no direct contact with the laser beam, leading to better cell viability, in addition to the production of significantly viscous products at fast speeds (Table 1). The disadvantages are the high costs of its operation and the need for further research to determine how practical it is in producing well-engineered tissue structures (Heinrich et al., 2019).

Table 1: The Different 3D Bioprinting Techniques, Advantages, and Disadvantages. (Table taken from Heinrich et al., 2019)



3D Bioprinting Technique	Advantages	Disadvantages
Stereolithography	- Simultaneous crosslinking of the whole 2D layer avoids need of X-Y movement - High cell viability (>85%) - High variety of printable bioinks - High resolution of bioprinting (~1 μm)	- Crosslinking requires transparent and photosensitive bioink limiting choice of additives and cell density (10^8 cells mL^{-1}) - Comparatively complex system
Inkjet Bioprinting	- Simple bioprinting method - Low cost - Applicability of multi-material bioprinting - High resolution (~30 μm) - High cell viability (80–90%)	- Limited to low cell density (<10^6 cells mL^{-1}) - Limited to bioinks with viscosity of 3.5–12 mPa·s
Laser-assisted Bioprinting	- High cell viability (>95%) - Variety of printable bioinks with viscosity of 1–300 mPa·s	- Limited to low cell density (<10^6 cells mL^{-1}) - Complex system - Comparatively high costs
Extrusion-based Bioprinting	- Printability of highly viscous bioinks (30–6×10^7 mPa·s) - Printability of high cell densities (including cell spheroids) - Applicability of multi-material bioprinting - Comparatively simple bioprinting process	- Relatively low printing speed - Low-to-medium resolution highly dependent on setup - Moderate cell viability (40–80%) dependent on setup
Electrospinning-based Bioprinting	- High resolution (<1 μm) - Optimal for the fabrication of scaffolds	- Not possible to directly bioprint cell-laden constructs - Complex system - High costs

The first report of using extrusion-based bioprinting was generated in 2002 by a team named “Hutmacher and co-workers”. It produces structures via melting poly(ε-caprolactone) (PCL) scaffolds through an extruding apparatus onto a collection platform. As shown in Figure 2, there are three kinds of strategies that are categorized under two classes. The first class is a fluid dispensing system that is pneumatically driven, and it is a pressure-based system divided into two kinds: valve-free or valve-based. The valve-free system is well-known in bioprinting due to its ease in manufacturing (Heinrich et al., 2019).

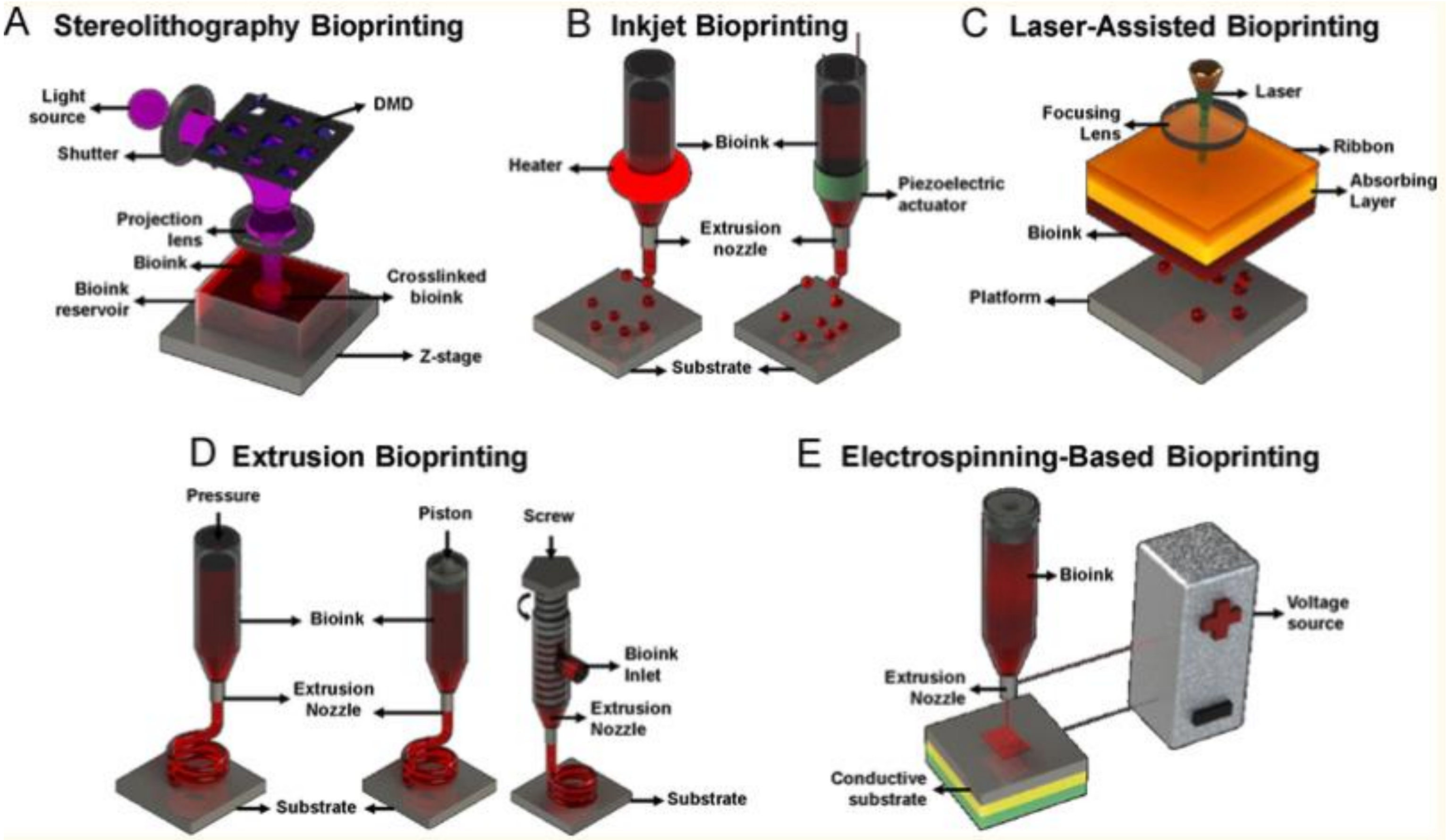


Figure 2: The Different 3D Bioprinting Techniques Utilized in Tissue Fabrication. The figure above projects various 3D bioprinting methods and their apparatuses. (A) Stereolithography with a DMD basis. (B) Two kinds of inkjet bioprinting, which are thermal (left) and piezoelectric actuation (right). (C) Laser-assisted bioprinting. (D) The three different methods of extrusion bioprinting. They are based on (from left to right) pressure, piston, and a screw. (E) Electrospinning-Based bioprinting (Figure taken from Heinrich et al., 2019).

On the other hand, the valve-based system is significantly precise in accumulating materials due to its properties in controlling pulse frequencies and pressures, leading to printed products with outstanding quality (Heinrich et al., 2019). The second class is mechanically driven, and it contains two systems, each controlled by either a piston or a screw. The screw-based system is best for highly viscous bioinks to maintain spatial control, whereas the piston-based system is best for managing the accumulation of bioink directly onto the collecting base of the apparatus (Heinrich et al., 2019).

The last bioprinting technique is the electrospinning-based bioprinting (EBB). It is a relatively new technique that requires further research and improvements. This technique is dedicated to the production of micro-sized materials via an electric force that may change into any state of matter. The particular reason behind the need for further improvements is due to a disadvantage experienced by this technique: rapid spinning that produces structures with low stability (Heinrich et al., 2019).

OBJECTIVES

Although there is not a consensus opinion on the 3D printing technology topic, it seems that there is a consensus on educating dental practitioners and students. An article published by Oberoi et al. (2018), stated that there had been an increasing trend in awareness of the applications of 3D printing in medicine and dentistry due to the increasing number of publications in the past 13 years. The specialists that are mainly involved in optimizing 3D printers in their practices are oral surgeons, prosthodontists, and orthodontists (Oberoi et al., 2018).

The objectives of this literature review are:

- Discuss the advantages and disadvantages of 3D printing
- Discuss the limitations that dental practitioners experience regarding the 3D printing technology
- List the top-rated 3D printers in terms of ease in use, cost-effectiveness, timesaving, and practicality overall
- Analyze the future projections of 3D printing, especially in tissue engineering, implantology, and Temporomandibular joint prosthesis

The goals above will enable the readers of this review to be educated and aware of the benefits of 3D bioprinting technology and its rapid advancement. Accomplishing these goals may potentially influence current and future dental practitioners to incorporate this technology in their practices, especially oral surgery and implant specialists.

PUBLISHED STUDIES

Advantages and Disadvantages of 3D Printing:

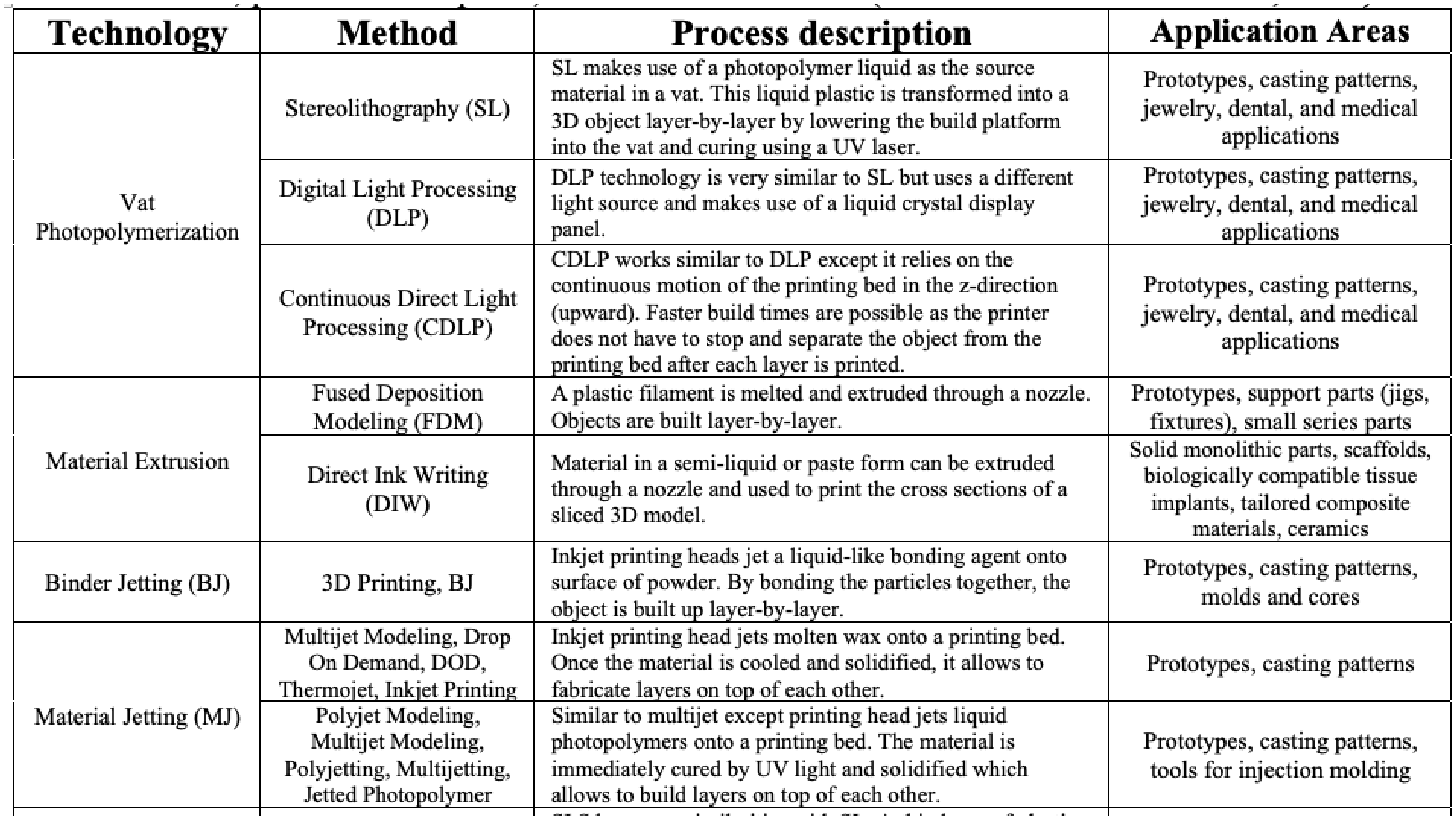
Tian et al. (2021) discuss their general opinions on 3D printers, claiming that by designing and producing specific structures, 3D printers modernized diagnosis and surgical treatments, in addition to the fabrication of customized prosthodontics that ensure positive postoperative results and reduced financial costs (Tian et al., 2021). Unfortunately, 3D printers are not free from challenges. The layer-by-layer superposition principle may cause products to undergo anisotropy; this sets limits when considering the long-term usage of intraoral tools, such as occlusal splints.

Additionally, the presence of layers impacts the consistency of the digital model to the entity, rendering the surface of equipment with high requirements for surface smoothness, such as ceramic restoration, unsuitable. It is also worth noting that 3D printing requires a mix of digital file capture hardware and computer-aided design (CAD) software. Adding to the mentioned disadvantages, the high cost of the equipment complicates popularizing 3D printing (Tian et al., 2021).

On the contrary, while contemporary 3D printers can quickly produce models, obtaining digital files takes time; hence, 3D printing is not practical to emergency visits. Additionally, the precision of printed models is slightly less than that of digital data. Moreover, several obstacles exist, such as a lengthy postprocessing procedure and a high material cost. Inadequate training of operators may potentially impede the use of 3D printing in medical settings. Meanwhile, 3D printing technology applies to a wide variety of sectors, and most machines now in use are not tailored for dentistry, making specific tasks inaccessible to medical personnel (Tian et al., 2021).

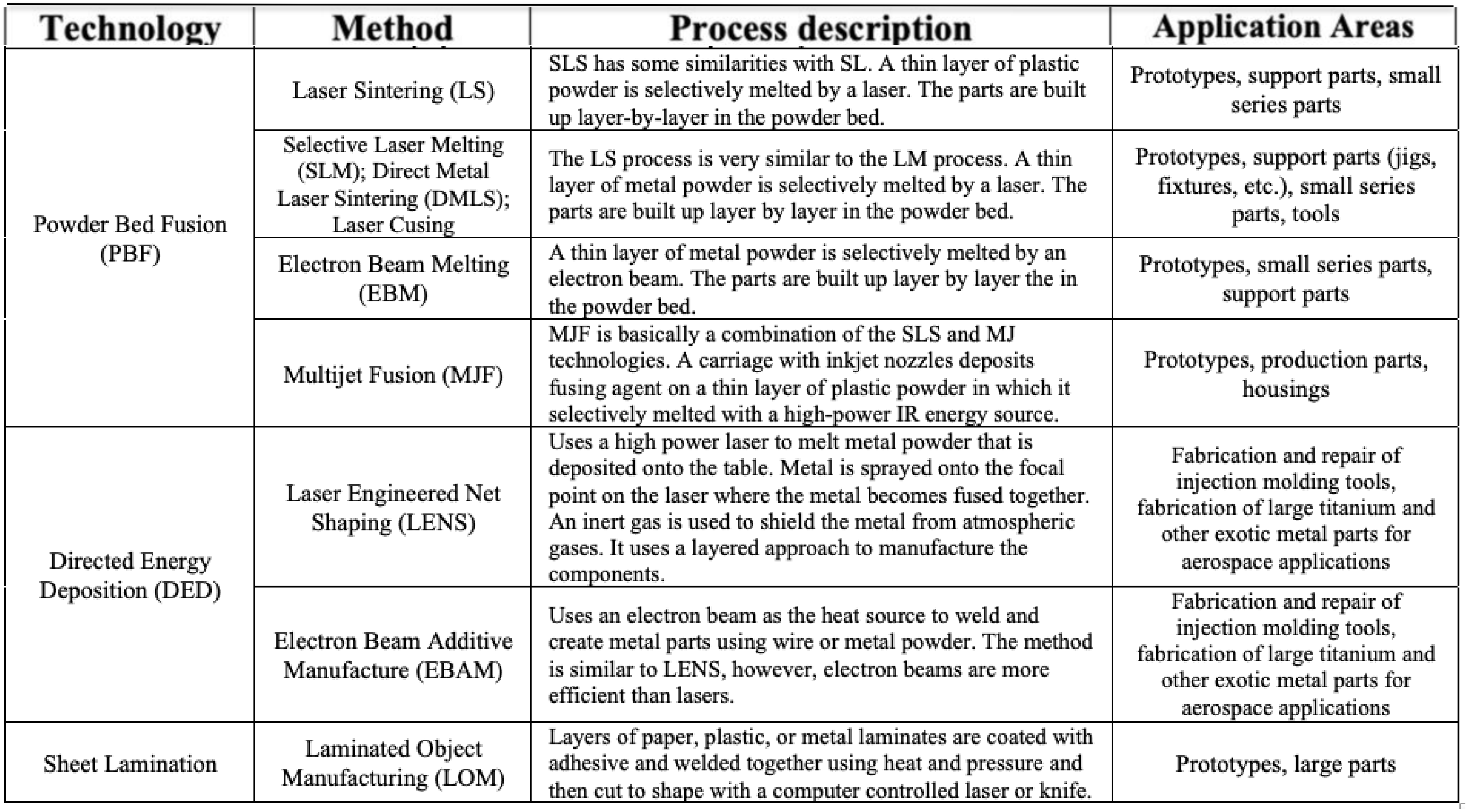
Tables 2A and 2B list the different forms of additive manufacturing technology, the methods used, their descriptions, in what industrial fields they are utilized, and the advantages and disadvantages of each method (Rafiee et al., 2020). Referring to Tables 2A and 2B, vat polymerization is the most appropriate class of 3D printing for medicinal purposes. Rafiee et al. (2020) made observations on the vat photopolymerization technology. They claim that it is unsuitable for multi-material 3D printing due to the incompletion of printing UV curable resins contained within a vat. Also, controlling contamination when different materials are used at once for production puts this technology at a disadvantage. What outweighs its deficiencies are its results with high resolution, precision in measurements, and supporting the use of various materials, each for different projects (Rafiee et al., 2020).

Table 2A: The AM Technologies. This table lists the different AM technologies, their methods, process description, and the areas utilized (obtained from Rafiee et al., 2020)



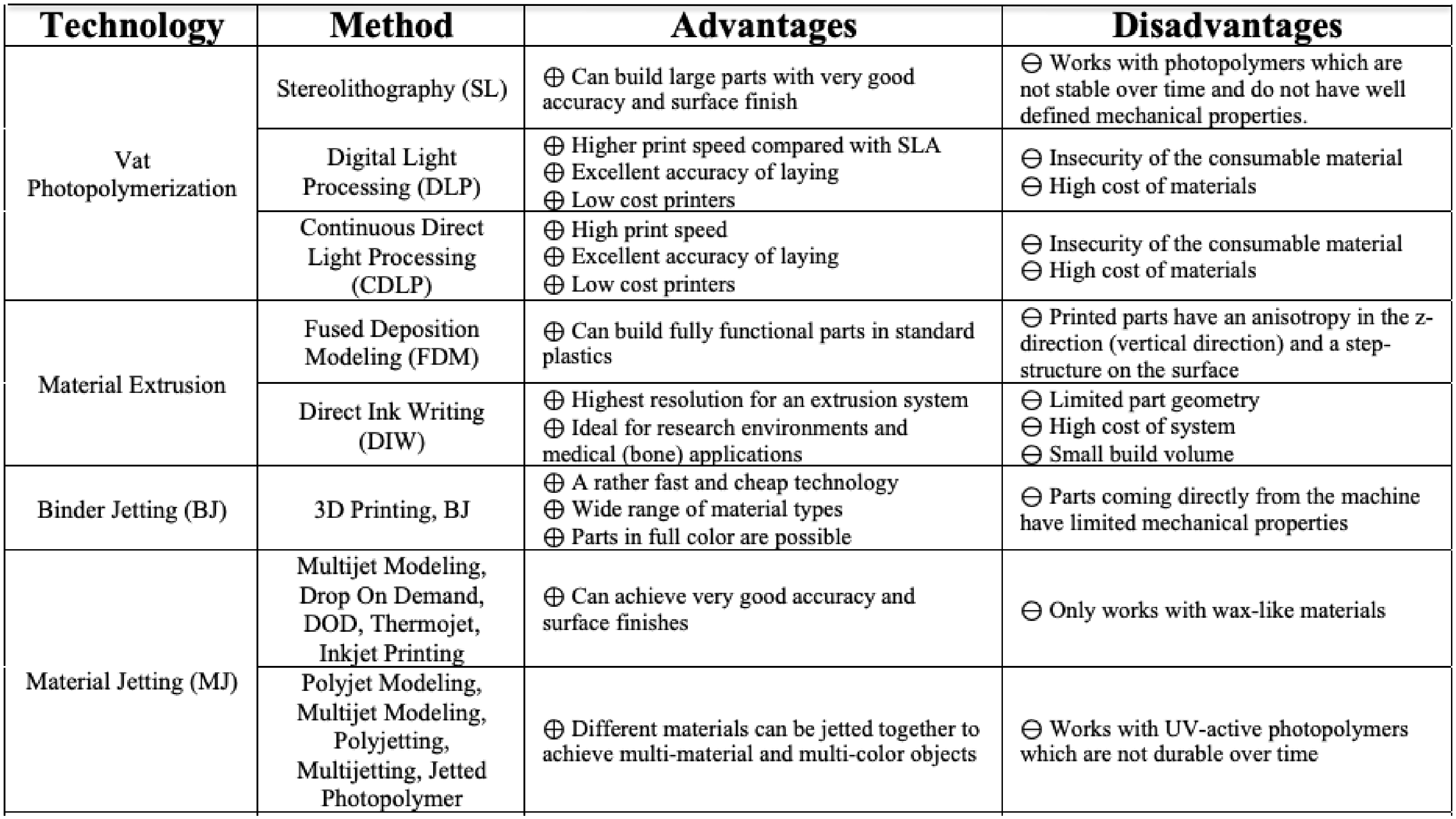
Technology	Method	Process description	Application Areas
Vat Photopolymerization	Stereolithography (SL)	SL makes use of a photopolymer liquid as the source material in a vat. This liquid plastic is transformed into a 3D object layer-by-layer by lowering the build platform into the vat and curing using a UV laser.	Prototypes, casting patterns, jewelry, dental, and medical applications
	Digital Light Processing (DLP)	DLP technology is very similar to SL but uses a different light source and makes use of a liquid crystal display panel.	Prototypes, casting patterns, jewelry, dental, and medical applications
	Continuous Direct Light Processing (CDLP)	CDLP works similar to DLP except it relies on the continuous motion of the printing bed in the z-direction (upward). Faster build times are possible as the printer does not have to stop and separate the object from the printing bed after each layer is printed.	Prototypes, casting patterns, jewelry, dental, and medical applications
Material Extrusion	Fused Deposition Modeling (FDM)	A plastic filament is melted and extruded through a nozzle. Objects are built layer-by-layer.	Prototypes, support parts (jigs, fixtures), small series parts
	Direct Ink Writing (DIW)	Material in a semi-liquid or paste form can be extruded through a nozzle and used to print the cross sections of a sliced 3D model.	Solid monolithic parts, scaffolds, biologically compatible tissue implants, tailored composite materials, ceramics
Binder Jetting (BJ)	3D Printing, BJ	Inkjet printing heads jet a liquid-like bonding agent onto surface of powder. By bonding the particles together, the object is built up layer-by-layer.	Prototypes, casting patterns, molds and cores
Material Jetting (MJ)	Multijet Modeling, Drop On Demand, DOD, Thermojet, Inkjet Printing	Inkjet printing head jets molten wax onto a printing bed. Once the material is cooled and solidified, it allows to fabricate layers on top of each other.	Prototypes, casting patterns
	Polyjet Modeling, Multijet Modeling, Polyjetting, Multijetting, Jetted Photopolymer	Similar to multijet except printing head jets liquid photopolymers onto a printing bed. The material is immediately cured by UV light and solidified which allows to build layers on top of each other.	Prototypes, casting patterns, tools for injection molding

Table 2A Continued: The AM Technologies. This table lists the different AM technologies, their methods, process description, and the areas utilized (obtained from Rafiee et al., 2020)



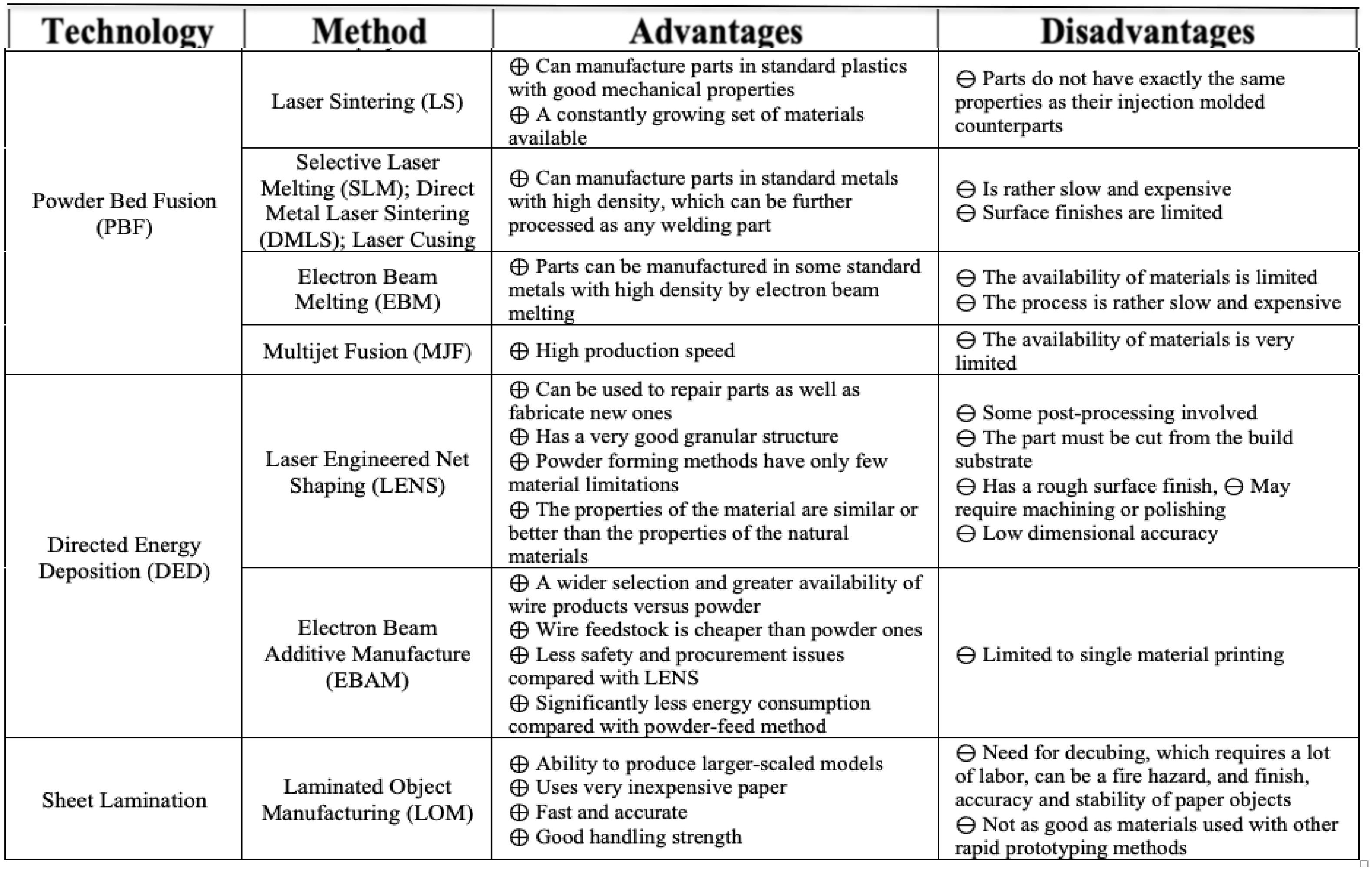
Technology	Method	Process description	Application Areas
Powder Bed Fusion (PBF)	Laser Sintering (LS)	SLS has some similarities with SL. A thin layer of plastic powder is selectively melted by a laser. The parts are built up layer-by-layer in the powder bed.	Prototypes, support parts, small series parts
	Selective Laser Melting (SLM); Direct Metal Laser Sintering (DMLS); Laser Cusing	The LS process is very similar to the LM process. A thin layer of metal powder is selectively melted by a laser. The parts are built up layer by layer in the powder bed.	Prototypes, support parts (jigs, fixtures, etc.), small series parts, tools
	Electron Beam Melting (EBM)	A thin layer of metal powder is selectively melted by an electron beam. The parts are built up layer by layer the in the powder bed.	Prototypes, small series parts, support parts
	Multijet Fusion (MJF)	MJF is basically a combination of the SLS and MJ technologies. A carriage with inkjet nozzles deposits fusing agent on a thin layer of plastic powder in which it selectively melted with a high-power IR energy source.	Prototypes, production parts, housings
Directed Energy Deposition (DED)	Laser Engineered Net Shaping (LENS)	Uses a high power laser to melt metal powder that is deposited onto the table. Metal is sprayed onto the focal point on the laser where the metal becomes fused together. An inert gas is used to shield the metal from atmospheric gases. It uses a layered approach to manufacture the components.	Fabrication and repair of injection molding tools, fabrication of large titanium and other exotic metal parts for aerospace applications
	Electron Beam Additive Manufacture (EBAM)	Uses an electron beam as the heat source to weld and create metal parts using wire or metal powder. The method is similar to LENS, however, electron beams are more efficient than lasers.	Fabrication and repair of injection molding tools, fabrication of large titanium and other exotic metal parts for aerospace applications
Sheet Lamination	Laminated Object Manufacturing (LOM)	Layers of paper, plastic, or metal laminates are coated with adhesive and welded together using heat and pressure and then cut to shape with a computer controlled laser or knife.	Prototypes, large parts

Table 2B: The AM Technologies. This table lists the different AM technologies, their methods, advantages, and disadvantages (obtained from Rafiee et al., 2020).



Technology	Method	Advantages	Disadvantages
Vat Photopolymerization	Stereolithography (SL)	⊕ Can build large parts with very good accuracy and surface finish	⊖ Works with photopolymers which are not stable over time and do not have well defined mechanical properties.
	Digital Light Processing (DLP)	⊕ Higher print speed compared with SLA ⊕ Excellent accuracy of laying ⊕ Low cost printers	⊖ Insecurity of the consumable material ⊖ High cost of materials
	Continuous Direct Light Processing (CDLP)	⊕ High print speed ⊕ Excellent accuracy of laying ⊕ Low cost printers	⊖ Insecurity of the consumable material ⊖ High cost of materials
Material Extrusion	Fused Deposition Modeling (FDM)	⊕ Can build fully functional parts in standard plastics	⊖ Printed parts have an anisotropy in the z-direction (vertical direction) and a step-structure on the surface
	Direct Ink Writing (DIW)	⊕ Highest resolution for an extrusion system ⊕ Ideal for research environments and medical (bone) applications	⊖ Limited part geometry ⊖ High cost of system ⊖ Small build volume
Binder Jetting (BJ)	3D Printing, BJ	⊕ A rather fast and cheap technology ⊕ Wide range of material types ⊕ Parts in full color are possible	⊖ Parts coming directly from the machine have limited mechanical properties
Material Jetting (MJ)	Multijet Modeling, Drop On Demand, DOD, Thermojet, Inkjet Printing	⊕ Can achieve very good accuracy and surface finishes	⊖ Only works with wax-like materials
	Polyjet Modeling, Multijet Modeling, Polyjetting, Multijetting, Jetted Photopolymer	⊕ Different materials can be jetted together to achieve multi-material and multi-color objects	⊖ Works with UV-active photopolymers which are not durable over time

Table 2B Continued: The AM Technologies. This table lists the different AM technologies, their methods, advantages, and disadvantages (obtained from Rafiee et al., 2020).



Technology	Method	Advantages	Disadvantages
Powder Bed Fusion (PBF)	Laser Sintering (LS)	⊕ Can manufacture parts in standard plastics with good mechanical properties ⊕ A constantly growing set of materials available	⊖ Parts do not have exactly the same properties as their injection molded counterparts
	Selective Laser Melting (SLM); Direct Metal Laser Sintering (DMLS); Laser Cusing	⊕ Can manufacture parts in standard metals with high density, which can be further processed as any welding part	⊖ Is rather slow and expensive ⊖ Surface finishes are limited
	Electron Beam Melting (EBM)	⊕ Parts can be manufactured in some standard metals with high density by electron beam melting	⊖ The availability of materials is limited ⊖ The process is rather slow and expensive
	Multijet Fusion (MJF)	⊕ High production speed	⊖ The availability of materials is very limited
Directed Energy Deposition (DED)	Laser Engineered Net Shaping (LENS)	⊕ Can be used to repair parts as well as fabricate new ones ⊕ Has a very good granular structure ⊕ Powder forming methods have only few material limitations ⊕ The properties of the material are similar or better than the properties of the natural materials	⊖ Some post-processing involved ⊖ The part must be cut from the build substrate ⊖ Has a rough surface finish, ⊖ May require machining or polishing ⊖ Low dimensional accuracy
	Electron Beam Additive Manufacture (EBAM)	⊕ A wider selection and greater availability of wire products versus powder ⊕ Wire feedstock is cheaper than powder ones ⊕ Less safety and procurement issues compared with LENS ⊕ Significantly less energy consumption compared with powder-feed method	⊖ Limited to single material printing
Sheet Lamination	Laminated Object Manufacturing (LOM)	⊕ Ability to produce larger-scaled models ⊕ Uses very inexpensive paper ⊕ Fast and accurate ⊕ Good handling strength	⊖ Need for decubing, which requires a lot of labor, can be a fire hazard, and finish, accuracy and stability of paper objects ⊖ Not as good as materials used with other rapid prototyping methods

3D Printer Limitations:

Many articles suggest there are certain limitations to the available 3D printers. Since the technology has been recently introduced to medicine, the slow progression in research and clinical trials is expected. Wilcox et al. (2017) conducted a review on the applications of 3D printing in spinal surgeries. The issues they listed were financial implications, the excessive amount of time allocated for manufacturing, and the selection of the appropriate materials (Wilcox et al., 2017). Another article by Cogswell et al. (2020) states that the technology is costly, with the deficiency of cases undergoing trials for 3D printing intracranial vascular tissues, and both factors contribute to insufficient statistical data (Cogswell et al., 2020).

Yang et al. (2019) discuss the developments in 4D bioprinting. 4D printing is a more advanced production technology based on 3D printing, in which the fourth dimension added is referred to as "time." When prompted by an external input, the printed structures may change form over time in this manner. The technology of 4D printing should be credited to "Skylar Tibbits" of the Massachusetts Institute of Technology (MIT), who produced multiple prototypes (Yang et al., 2019). 4D bioprinting is a process in which the printed bioconstructs may alter over time. 4D bioprinting's defining trait is "changing" in terms of either size, shape, or usefulness (Figure 3). The objects may grow or contract in response to the change in size. In most situations of 4D bioprinting, the printed objects are capable of deforming into new forms when stimulated externally. For example, an initially flat structure may grow in a controlled way into various geometries. Another sort of 4D bioprinting is a functional change, which refers to the evolution of live cells, including cell fusion, cell assembly, and other biological characteristics (Yang et al., 2019).

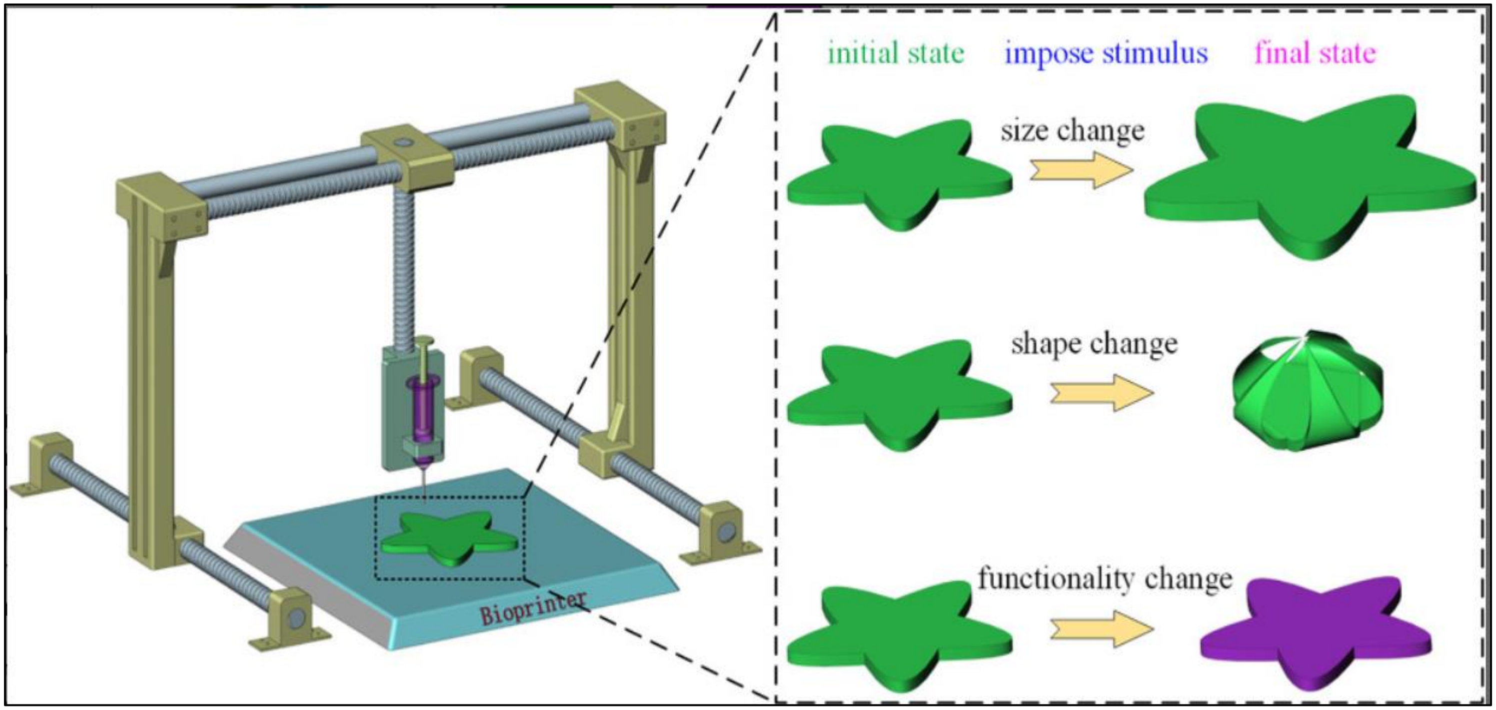


Figure 3: A Demonstration of 4D Bioprinting. This figure projects how a fabricated structure (via a 4D bioprinter) may experience possible alterations in its characteristics. With the fourth dimension as "time", the structure may be stimulated to change in shape, size, and properties (Figure from Yang et al. 2019).

The limitations presented included the software design of the structures. Currently, there is a lack of computational models capable of precisely predicting the evolution of 4D bioprinted products. Thus, the structure's design is determined chiefly by experimental attempts and empirical data. Another obstacle to 4D bioprinting is the development of materials or bioinks. The materials used in 4D bioprinting may be classified into two groups based on their mechanical properties: soft and hard materials (Yang et al., 2019).

Biocompatibility is high for soft materials (e.g., hydrogels), while mechanical properties, such as rigidity, are low. Some researchers employed hard materials in 4D bioprinting, which have good mechanical properties but are not verified for biocompatibility (Yang et al., 2019). The ideal materials needed to conduct 4D bioprinting should be solid and biocompatible. Furthermore, the materials must be sensitive to external stimuli. Until now, the majority of materials have been sensitive to a single stimulus. However, the *in vivo* environment is complex, with many possible stimuli. As a result, it is necessary to produce materials that respond to various stimuli (Yang et al., 2019).

The emphasis on perfecting the CAD/CAM technology in dentistry has been reported as a necessity for avoiding surgical complications. Al-Ardah et al. (2018) presented a clinical report on their utilization of a virtual ridge augmentation and 3D printing to produce a positioning structure for a titanium mesh (TiMe) needed for bone grafting a patient's medial maxillary bone defect. As shown in Figures 4 and

5, cutting-edge imaging and software structural design are crucial to ensure effectiveness and immunity from any surgical complications. Without advanced cone beam computed tomography (CBCT) and CAD/CAM technologies, predictions pertaining to negative postoperative consequences may occur. Examples reported were the exposure of the membrane during the healing phase is the most commonly reported consequence of inappropriate TiMe usage or manufacture (Al-Ardah et al., 2018). One source of this exposure is soft tissue irritation induced by the TiMe's rough edges, resulting from the necessary cutting and bending to make a well-adapted TiMe. Additional reasons include an inability to achieve tension-free closure, a challenging suturing approach, and contamination leading to infection (Al-Ardah et al., 2018).

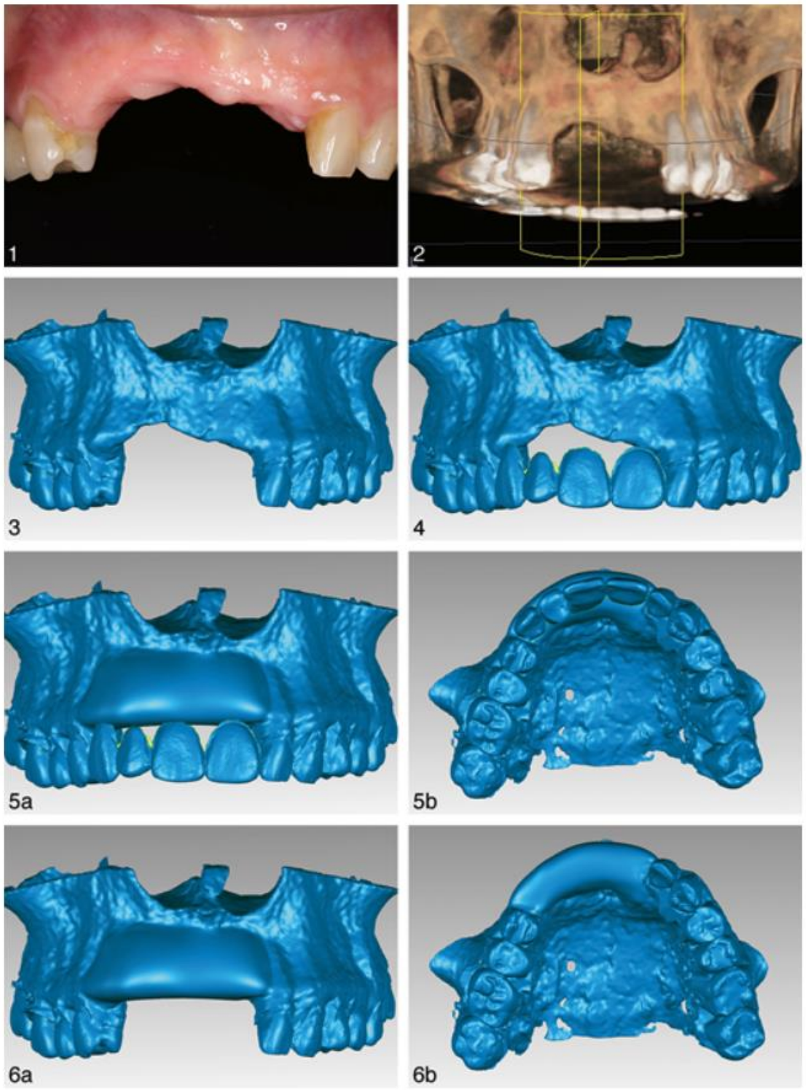


Figure 4: Projections of Advanced CBCT and CAD/CAM Tools of a Maxilla. This figure depicts screenshots and images from the clinical report made by Al-Ardah et al. (2018). (1) A picture of the patient's alveolar defect. (2) a CBCT scan of the defected area integrated into a measuring software. (3 – 6b) virtually designed 3D-imaging projecting the damaged area first, ending with designing the planned 3D virtual ridge augmentation (Figure taken from Al-Ardah et al., 2018).

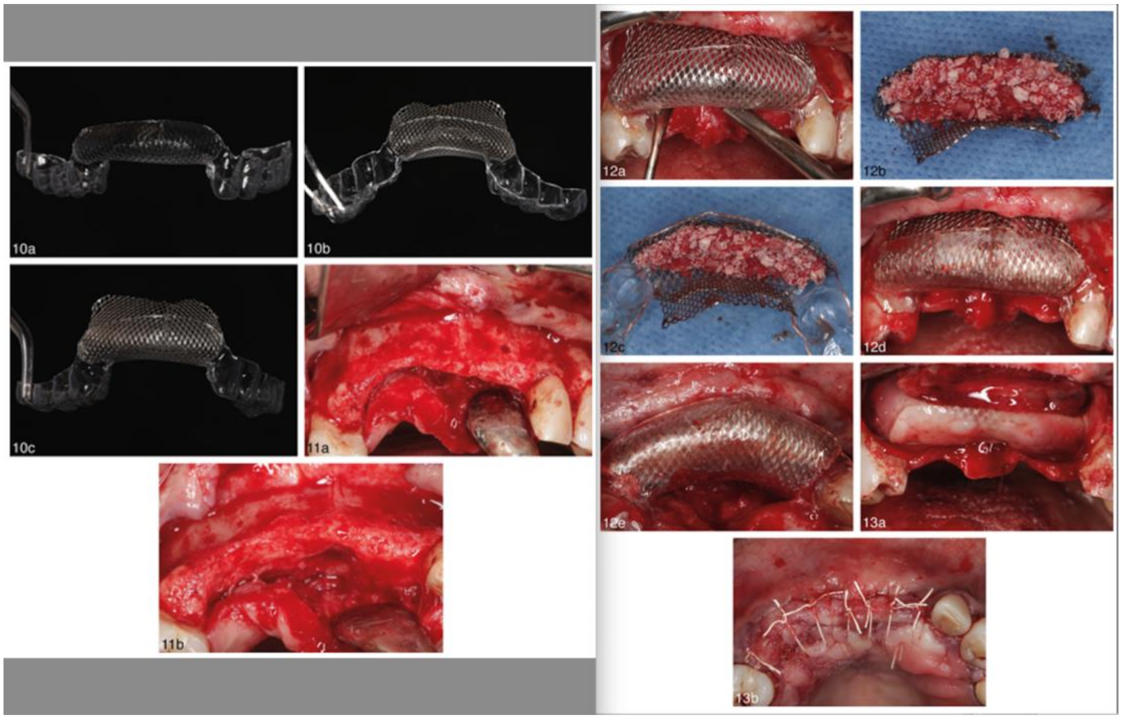


Figure 5: TiMe Positioning Aligner and The Ridge Augmentation Procedure. This figure shows images taken of the 3D printed TiMe positioning aligner, along with the pictures of the surgical site, starting with the early stages of the bone graft procedure and ending with the sutured site of the ridge augmentation (Figure taken from Al-Ardah et al., 2018).

Top-Rated 3D Printers:

Many companies produce 3D printers for different applications. Some of the top-rated printers being utilized today in dentistry are listed in Table 3. According to Schwaar (2021), the GE-Concept Laser is the preferred 3D printer for dental labs and practices. The industrial “Mlab” and “Mlab R” are 3D printers utilized in dental laboratories to produce complicated, personalized, and tension-free dental frames and prostheses. The Mlab printer prints extraordinarily detailed dental implants using metal powder (powder bed fusion technique).

GE offers this metal approach as a substitute for milling metal dental components, claiming that milling loses up to 85% of the material utilized in the production process. Furthermore, 3D printing is faster than metal casting, with a density of 99.6%. GE’s Dental Hybrid Manufacturing solution is developed in collaboration with Follow-Me, Datron, and Fresdental milling machines. It also combines the benefits of AM and SM with a common software platform that manages its 3D printing and milling features (Schwaar, 2021).

Table 3: List of Different Dental 3D Printing Brands. The table includes print types, names, technologies, and price range (table obtained from Schwaar, 2021)

Brand	Print Types	Printer	Technology	Price Range
Carima IMD	Models, surgical guides, provisional restorations, removable partials, wax-ups, temporary crowns and bridges, castable parts	IMD	DLP	$12,000
Shining 3D	Model, wax-ups, surgical guides, gingiva, customized impression trays, bracket transfer trays	AccuFab-D1s	DLP	N/A
Carbon	Models, denture bases, carded teeth, splints, night guards, surgical guides, temporary crowns and bridges, trays, gingiva masks	L1, M2, M2d	Digital Light Synthesis (DLS)	$50,000 - $100,000
3D Systems	Models, denture bases, castable parts, custom trays, surgical guides, orthodontic splints, crowns and bridges, removable frameworks, crown and bridge copings	NextDent 5100, ProX DMP 200 Dental	DLP	$ 5,000 - $ 10,000
Kulzer	Night guards, custom impression trays, surgical guides, models, CAD-to-cast structures	Cara Print 4.0	DLP	$15,000 - $20,000
SprintRay	Models, surgical guides, custom night guards, crowns, copings, bridges, RPDs	MoonRay, Pro	DLP	$4,000 - $6,750

Table 3 Continued: List of Different Dental 3D Printing Brands. The table includes print types, names, technologies, and price range (table obtained from Schwaar, 2021)

Brand	Print Types	Printer	Technology	Price Range
Asiga	Models, dental orthodontics, crown and bridge, surgical guides, custom trays, partial dentures, clear dental splints, castable parts for crown and bridge and frameworks	MAX series, Pro 4K	DLP	$9,000 - $25,000
Desktop Health EnvisionTEC	Models, surgical guides, provisional restorations, removable partials, wax-ups, temporary crowns and bridges, castable parts	Envision One, VECTOR 3SP, VIDA, D4K Pro	DLP; Continuous Digital Light Manufacturing (cDLM)	$10,000 - $50,000
GE - Concept Laser	Metal bridges and crowns	mLab	Direct Metal Laser Melting (DMLM)	$250,000
Formlabs	Models, aligners, surgical guides, occlusal splints, denture bases, denture teeth	Form 3B, Form 3BL	Low-force stereolithography (LFS)	$4,000 - $14,000
Stratasys	Models, surgical guides, night guards, castable partial denture frameworks, try-ins for veneers and dentures, orthodontic appliances, custom trays	J5 DentaJet, Objet260 Dental, Objet Eden 260VS Dental Advantage, Objet30 Orthodesk, Stratasys J700 Dental	PolyJet	$100,000-$250,000

Table 3 Continued: List of Different Dental 3D Printing Brands. The table includes print types, names, technologies, and price range (table obtained from Schwaar, 2021)

Brand	Print Types	Printer	Technology	Price Range
Trumpf	Metal bridges and crowns	TruPrint 1000	Selective Laser Melting (SLM)	$170,000
Zortrax	Patterns of crowns and bridges, clear aligners, surgical guides, occlusal splints	Inkspire	SLA	$1,700
Rapid Shape	Models, surgical guides, provisional restorations, removable partials, wax-ups, temporary crowns and bridges, castable parts	D10, D20, D30, D40, D70, D90	SLA	$10,000 - $50,000
Nexa3D	models, surgical guides, gingiva, customized impression trays, bracket transfer trays	NXD 200	SLA	$30,000

Tissue Engineering:

The integration of cells and biomaterials using bioprinting and microfluidic technologies is expected to create novel microenvironments for a variety of applications in cancer biology, tissue engineering, and regenerative medicine. Additionally, advances in high-throughput biomanufacturing of three-dimensional designs will open the door for additional innovations of *in vitro* screening and diagnostic applications, possibly enabling the fabrication of sophisticated organ constructions (Arslan-Yildiz et al., 2016)

3D printing biotechnologies have transformed the old standard of fabricating artificial dental tissues, and 3D bioprinting is accelerating the advancement of this subject. By printing all components, cells, and matrix materials, 3D bioprinting enables the production of biostructures that are more similar to normal dental tissues. This is accomplished by managing both the internal and exterior features of the regenerated modules. Nonetheless, the application of 3D bioprinting in the regeneration of teeth and supporting tissue is an innovative domain that faces numerous barriers. An example is the development of suitable biomaterials for dental tissues' soft and hard components and optimizing printing processes for increased cytocompatibility. Additionally, the application of biological printing to dental stem cells is new and beginning to grow rapidly. Nevertheless, the combination of dental cellular biology and mechanical engineering can fulfill this technology's full potential in both research and clinical settings (Ma et al., 2019).

Nesic et al. (2020) claim that comparable artificial periodontal tissue serves as the foundation for prospective 3D-printed intraoral soft tissue grafts. Artificially structured gingiva, with the appropriate thickness, should contain elements including a supporting connective tissue (i.e., lamina propria) containing fibroblasts within a vascularized Extracellular matrix. It should also consist of a continuous basement membrane, acting as a border between the lamina propria and the epithelium. The last element included in the aforementioned structured gingiva is a stratified squamous epithelium, which envelopes keratinocytes that are densely inserted and experience alterations as they migrate superficially. Scaffolds produced and employed in manufacturing artificial gingiva may be categorized as naturally extracted (for example, an acellular human dermis), or derived from collagen, fibrin, gelatin, or synthetic (polycaprolactone, PCL) or hybrid (Nesic et al., 2020).

In contrast to *in vitro* research, which frequently favored immortalized cell lines for the purpose of availability, repeatability, and uniformity, for clinical applications, cells extracted from autologous biopsies were the major cell source. On the other hand, cancer-derived cell lines frequently have impaired physiological responses (Nesic et al., 2020). Thus, via overexpression of Telomerase Reverse Transcriptase, keratinocytes and fibroblasts were rejuvenated in a physiological sense. These organotypic structures are essential for studying the biological aspects of the oral mucosa. They are employed in labs to help comprehend the biological functions of the human oral mucosa barrier qualities as well as various defects, such as oral cancer and microbial infections (Nesic et al., 2020).

As shown in Figure 6, 3D printing would enable the act per a sequence of steps, which would induce the fabrication of customized tissues. Several actions should be performed to initiate the oral mucosa 3D printing technique: acquiring proper scans and images, selecting bioinks that are biologically, chemically, and mechanically compatible. Other actions to take into consideration are the printing method and the inclusion or exclusion of cells (with their origin) (Nesic et al. 2020). The Haptics technology, which is the technology that one may use to transmit, comprehend, and interact (via human touch) virtually, has enabled digital projection of bone, gingiva, and vasculature during arranging treatment plans for facial reconstruction operations. The degree and structure of tissue defects and the vasculature of a concerned area may be assessed using the intraoral scan digital capture (Nesic et al., 2020).

Biocompatibility, high absorbency to facilitate cell population, tissue regeneration, vascular construction, biodegradability proportional to the rate of new matrix deposition (tissue generation), and mechanical stability are all desirable properties of 3D printable biomaterials. Appropriate macro-architecture qualities would ensure that neovascularization occurs promptly. Continuous growth and adaption of the capabilities of 3D printers, together with lower costs, improved speed, and the usage of a broader range of printable materials, will propel this innovation towards the frontline of biomedical applications. As more academics with diverse backgrounds and research objectives utilize 3D printers, new difficulties, requirements, and achievements are feasible in the bioprinting realm. Abiding by the envisioned series of steps (as shown in Figure 6) to create a customized graft with an altered inner layout and exterior shape may enhance tissue-mimicking results in functional and aesthetically satisfying soft tissue augmentation (Nesic et al., 2020).

By considering the heterogeneity in the form, inner anatomy, thickness, volume, dynamics, and functionality of soft tissue correlated with its placement in the intraoral cavity, 3D printing may demonstrate to be a suitable technique for creating scaffolds for soft tissue grafting. Notably, 3D printing would facilitate abiding by a sequence of steps (Figure 6), which would lead to the fabrication of customized artificial soft tissue. The perpetual development and adaption of 3D printers' features, alongside lower prices, improved speed, and the ability to print a wider variety of artificial structures, will propel this technology to the frontline of clinical applications (Nesic et al., 2020).

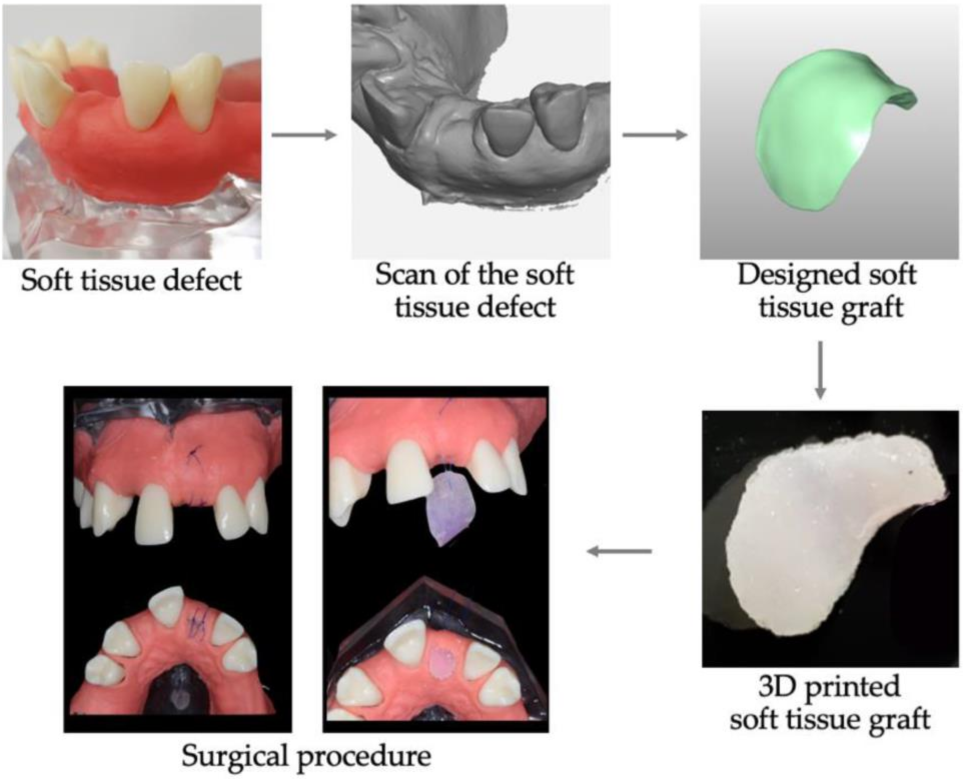


Figure 6: The Potential Protocol for Soft Tissue Grafting in The Future. This figure depicts a predicted method of intraoral soft tissue implantation using a 3D bioprinted artificial soft tissue graft. Starting with obtaining intraoral scans and CBCT imaging, following with CAD/CAM designing of the tissue graft, printing, and lasting with performing the surgical procedure (Obtained from Nesic et al., 2020).

Implantology:

Bioprinting enables advanced bioengineered constructions with the potential to offer enhanced tooth loss remedies in the near future and experimental models that will advance the field. Bioprinting will address the current clinical requirement for dependable dental implants with an intelligent choice of material and scaffold design in combination with widely obtainable cells. Additionally, as technology advances, dental and periodontal regeneration options will expand exponentially, including hitherto unimagined solutions for dental and periodontal regeneration (Morrison and Tomlinson, 2021).

Strbac et al. (2016) describe a technique as the use of digitally designed 3D printed surgical templates for guided osteotomy preparation and safe implantation of donated teeth. This revolutionary technology presented a completely automated digital workflow for accurate pretreatment planning and guided osteotomy during autotransplantation for the first time (Strbac et al., 2016). This strategy might be used to apply all recommended protocols and surgical techniques using unique surgical templates, guaranteeing an atraumatic treatment experience by protecting soft and hard tissues and avoiding harm to fragile dental structures. By utilizing precise 3D printed templates, this technology may aid in the completion of exceedingly difficult surgical and prosthodontic operations, hence increasing the success rate of future autotransplants (Strbac et al., 2016).

Temporomandibular Joint Prosthesis:

Zheng et al. (2019) conducted a clinical study revolving around the temporomandibular joint (TMJ) prosthesis via designing and 3D printing customized artificial TMJ. Figure 7 depicts the process of designing and manufacturing the artificial TMJ studied in this clinical report. Total TMJ prosthesis is a safe and effective way of reconstructing the joint. However, there was an urgent need to develop a new TMJ prosthesis due to the lack of commercially available prostheses suitable for clinical usage in the Chinese population. The main objective of this study was to prospectively validate the safety and efficacy of a novel TMJ prosthesis with customized design and additive manufacturing using 3D printing in a clinical application (Zheng et al.2019).

The research enrolled 12 consecutive participants. There were no postoperative problems (infection of the surgical site, liver and kidney damage, displacement, breaking, or loosening of the prosthesis). Following surgery, pain, diet, mandibular function, and maximum interincisal opening all improved substantially. However, lateral mobility was restricted to the non-operated side, and when the mouth was opened post-surgery, the jaw deviated towards the operated side (Zheng et al., 2019).

The provided TMJ prosthesis is regarded as a new product in the TMJ Yang's system since it is distinctive compared to previous prostheses due to its unique design and additive manufacturing process using 3D printing. Additionally, the prosthesis is exceptionally safe and effective in clinical settings. This study will bolster the case for the revolutionary prosthesis's widespread clinical application in the future (Zheng et al., 2019).

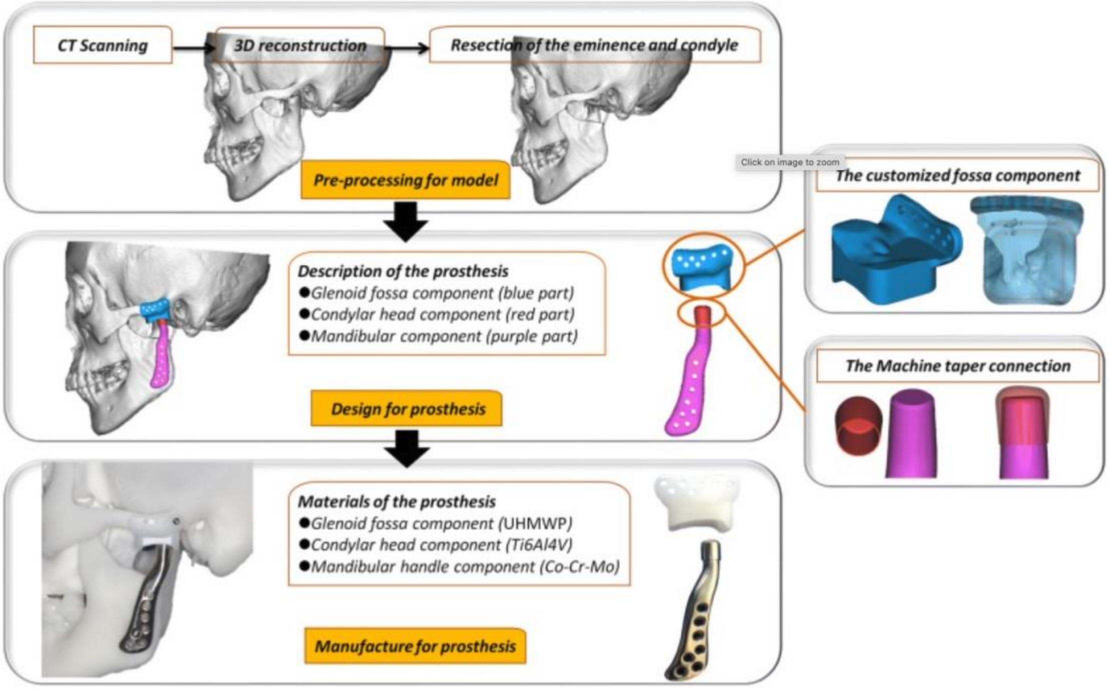


Figure 7: The Steps of TMJ Prosthesis Manufacturing. This includes pre-processing the craniomaxillofacial model, designing the prosthesis, and manufacturing the structure. The tailored fossa component with a single UHMWP and the Machine tape mechanism for connecting the condylar head (Co–Cr–Mo alloy) and mandibular handle components are the prosthesis's primary innovations (Ti6Al4 V alloy) (Figure taken from Zheng et al., 2019)

DISCUSSION

3D printing technology is an exciting field that continues to grow exponentially being used for dental prosthetics, oral appliances, tissue engineering and more; however, as with any new advance there is still much to learn to maximize its potential.

The limitations section of this review provided insight into several significant areas that deserve attention. For instance, Al-Ardah et al. (2018) stated that computer applications and designing software play an integral role in the accuracy and precision of the construction and use of the 3D printers' products in surgical applications. The importance of advanced scanning equipment and processing software (CBCT, CAD/CAM) was emphasized since any errors in scans and measurements pertaining to a surgical area, for example, may lead to unwanted surgical complications and potential harm to patients. One of the main goals behind the use of 3D printers in medicine is to manufacture artificial prosthodontics, tissues, organs, and other desired products explicitly customized for each patient and ideally with minimal error. As noted earlier, this is critical as the uniqueness of each patient must not be disregarded.

Furthermore, Tian et al. (2021) conclude that a 3D printer may be compromised if its operators are poorly trained. This conclusion leads to the emphasis on the fact that whoever is responsible for operating said machinery must undergo thorough training and obtain certification upon completion. Also, in the future, it may be beneficial to issue licenses for operators that expire after a set period, and the renewal of licenses may only occur upon completing several hours of continuing education courses. This would allow for updated training in alignment with updates and breakthroughs in the research and advancement of 3D printing.

Nesic et al. (2020) raised crucial points pertaining to the future of 3D printing of artificial soft tissue. Instead of conducting experiments on animals for drug targeting, vaccine synthesis, and conducting trials for novel treatments, the 3D printed artificial tissues make a stellar substitute (Nesic et al., 2020). Pharmacologists must be involved in the development of the bioprinted artificial soft tissues; since the requirement of antibiotics, immunoregulatory, and anti-inflammation medication may occur to prevent pathologies from arising, such as necrosis, inflammation, or infection (Nesic et al., 2020). Such technology may require similar approaches to organ transplants since artificial foreign structures will be introduced instead of naturally donated anatomical structures.

Tasnim et al. (2018) expands on the comparison between implanting and transplanting 3D bioprinted (artificial) and natural (donated) organs, respectively. The rejection of an immune system is a concern associated with organ transplants and highlights the importance of locating a tissue match donor. These concerns may be resolved by 3D bioprinting tissues or organs utilizing stem cells isolated from the patient's own body to create a substitute for the damaged organ. Using cost-effective bioprinter and bioink materials, it is conceivable to bioprint layer-by-layer organs or tissue. Thus, 3D bioprinting has enormous potential for delivering superior results in treating various critical illnesses straightforwardly and cost-effectively (Tasnim et al., 2018). Another area of future development is in the regeneration of teeth, especially enamel since it is one of the scarce biomaterials available. Another potential opportunity for usage is the incorporation of genetic processing and duplication of DNA to derive structuring of tissues, and possibly organs, of patients. This will be the ultimate form of customized treatments and could avoid encountering autoimmune reactions towards what could have been foreign structures.

There is a consensus among the scientific community that there is the need for continued research on the performance of 3D printers in medical applications. These studies should be completed broadly both in the US and globally, especially in in third-world countries, where medical and dental care is necessary. There may be challenges when conducting clinical studies of significant size and power due to fiscal limitations however corporations should consider providing opportunities to lend or reduce the costs of their inventions for the scientific community. In the long run, 3D printing holds great promise in advancing medical care overall and improving the quality of healthcare for many in the future.

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